Claims

1. A particle for transfecting higher eucaryotic cells with nucleic acid molecules *in vitro* and *in vivo* comprising one or more nucleic acid molecules condensed by organic cationic molecules, said particles being obtained by complexing the nucleic acid molecules with identical or different organic cationic precursor molecules without crosslinking nucleic acid molecules, and covalently linking the precursor molecules to each other on the the nucleic acid template.

2. The transfection particle of claim 1, wherein the cationic molecules are lipids obtained by dimerization or oligomerization of cationic detergent precursor molecules.

3. The transfection particle of claim 2, wherein the cationic detergent precursor molecules comprise:

   a) at least one function for binding to one or more other detergent molecules,
   b) at least one lipophilic residue,
   c) a non-toxic recipient backbone,
   d) a cationic group for binding to nucleic acid molecules.

4. The transfection particle of claim 3, wherein the function of the cationic precursor detergent molecules for binding to other detergent molecules is a dimerizable or polymerizable function selected from

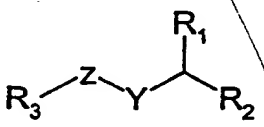
thiols, acid hydrazides, aldehydes, amines, and ethylene residues that are suitably substituted to provide enamines.

5. The transfection particle of claim 4, wherein the lipophilic residue is selected from lipophilic amides, esters or ethers.

6. The transfection particle of claim 3, wherein the function for binding to nucleic acid molecules is selected from an amine or derivative thereof.

7. The transfection particle of claim 6, wherein the function for binding to nucleic acid molecules is guanidine.

8. The transfection particle of claim 1, wherein the organic cationic precursor molecule is represented by general formula I



(I)

wherein

R_1 denotes (C_1-C_{10}-alkylene)-SH, wherein the alkylene radical may represent a straight chained or branched hydrocarbon;

R_2 denotes $-NR_4R_5$, $-NHR_4R_5^+$, $-N(R_4)_2R_5^+$, $-C(=NR_4)NR_5R_6$, $-C(=X)-C_1$-C_{10}-alkylene, wherein the alkylene radical may represent a straight chained or branched hydrocarbon and may be substituted by up to four dialkyl amino groups or a thiomonosaccharide;

R_3 denotes C_5-C_{30}-alkyl, straight chained or branched and

optionally substituted preferably with one or more halogen atom(s) or dialkyl amino group(s), or

C_5-C_{30}-alkenyl, straight chained or branched having up to ten C=C-double bonds and is optionally substituted preferably with one or more halogen atom(s) or dialkyl amino group(s), or

C_5-C_{30}-alkinyl, straight chained or branched having up to ten C≡C-triple bonds and is optionally substituted preferably with one or more halogen atom(s) or dialkyl amino group(s), or

C_6-C_{10}-aryl optionally substituted, or

C_7-C_{16}-aralkyl optionally substituted, or a

C_5-C_{30}-alkyl-chain interrupted by up to 10 amino groups $-NR_4-$ and having optionally an amino-group which is optionally substituted by an amino acid;

R_4, R_5 and R_6 denote independently from each other hydrogen or C_1-C_4-alkyl;

X denotes O or S;

Y denotes C=O or C=S and

Z denotes O, S or $-NR_4-$.

9. The transfection particle of claim 8, wherein the cationic precursor molecules correspond to general formula I, wherein

R_1 denotes (C_1-C_6-alkylene)-SH, wherein the alkylene radical may represent a straight chained or branched hydrocarbon;

R_2 denotes $-NR_4R_5$, $-NHR_4R_5^+$, $-N(R_4)_2R_5^+$, $-C(=NR_4)NR_5R_6$, $-C(=X)-C_1$-C_4-alkylene, wherein the alkylene radical may represent a straight chained or branched hydrocarbon and may be substituted by up to four amino radicals $-NR_4R_5$ or a thiomonosaccharide;

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R_3 denotes C_5-C_{20}-alkyl, straight chained or branched and optionally substituted preferably with F, Cl, Br or $-NR_4R_5$, or

C_5-C_{20}-alkenyl, straight chained or branched having up to five C=C-double bonds and is optionally substituted preferably with F, Cl, Br or $-NR_4R_5$, or

C_5-C_{20}-alkinyl, straight chained or branched having up to five C≡C-triple bonds and is optionally substituted preferably with F, Cl, Br or $-NR_4R_5$, or

C_6-C_{10}-aryl optionally substituted preferably with C_1-C_4-alkyl ,F, Cl, Br or $-NR_4R_5$, or

C_7-C_{14}-aralkyl optionally substituted preferably with C_1-C_4-alkyl, F, Cl, Br or $-NR_4R_5$, or

a C_5-C_{20}-alkyl chain interrupted by up to 10 amino groups $-NR_4-$ and having optionally a -amino-group which is optionally substituted by an amino acid;

R_4, R_5 and R_6 denote independently from each other hydrogen or C_1-C_4-alkyl;

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X denotes O or S;

Y denotes C=O or C=S and

Z denotes O, S or $-NR_4-$.

10. The transfection particle of claim 8, wherein the cationic precursor molecules correspond to general formula I, wherein

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R_1 denotes (C_1-C_4-alkylene)-SH, wherein the alkylene radical may represent a straight chained or branched hydrocarbon;

R_2 denotes $-NR_4R_5$, $-NHR_4R_5^+$, $-N(R_4)_2R_5^+$, $-C(=NR_4)NR_5R_6$, $-C(=X)-C_1-C_4$-alkyl, wherein the alkyl radical may represent a straight chained or branched hydrocarbon and may be substituted by up to four amino radicals $-NR_4R_5$, or a thiomonosaccharide;

R_3 C_5-C_{12}-alkyl, straight chained or branched and optionally substituted preferably with F, Cl, Br or $-NH_2$, or a

C_5-C_{15}-alkyl chain interrupted by up to 7 amino groups $-NR_4-$ and having optionally a -amino-group which is optionally substituted by the amino acid cysteine;

R_4, R_5 and R_6 denote independently from each other hydrogen or methyl, ethyl, propyl, iso-propyl, n-butyl, iso-butyl or tert.-butyl;

X denotes O or S;

Y denotes C=O or C=S and

Z denotes O, S or -NR_4-.

11. The transfection particle of claim 8, wherein the cationic precursor molecules correspond to the general formula I, wherein

R_1 denotes -CH_2-SH;

R_2 denotes -NH_2, -NH_3^+, -$C(=N^+H_2)NH_2$, -C(=O)-C_1-C_4-alkyl straight chained or branched and optionally substituted with F, Cl, Br or -NH_2,
or an ornithine radical or a S-galactosyl radical;

R_3 denotes a C_6-C_{15}-alkyl radical straight chained or branched and optionally substituted preferably with F, Cl, Br or -NH_2;

Y denotes C=O;

Z denotes O or -NH-.

12. The transfection particle of one of ~~claim 8~~ claims 8 to 11, wherein R_2 is guanidine ornithine.

13. The transfection particle of one of claim 8 to ~~12~~ 11, wherein R_3 is a decyl radical.

14. The transfection particle of one of ~~claim~~ claims 8 to 11, wherein R_1 is a methylenethiol, R_2 is a guanidine, R_3 is a straight chained decyl radical, Y is a carbonyl, Z is an amine, and pharmaceutically acceptable salts thereof.

15. The transfection particle of claim 14, wherein the cationic molecule is N-decyl-2-guanidinium-cysteine.

16. The transfection particle of one of claim 8 to 11, wherein R_1 is a methylenethiol, R_2 is an ornithine, R_3 is a decane, Y is a carbonyl, Z is an amine, and pharmaceutically acceptable salts thereof.

17. The transfection particle of claim 16, wherein the cationic molecule is N-decyl-2-ornithinyl-cysteine.

18. The transfection particle of one of claim 8 to 11, wherein the monosaccharide which is bonded via a sulfur atom is selected from the group consisting of galactose, lactose, glucose, arabinose , fructose, sorbose, xylose, ribose, mannose each of them in their D- or L-form.

19. The transfection particle of claim 1, wherein the cationic precursor molecule is a polyamine.

20. The transfection particle of claim 19, wherein the cationic precursor molecule is a spermine derivative.

21. The transfection particle of claim 20, wherein the cationic precursor molecule is spermine-N1,N12-bis-cysteineamide.

22. The transfection particle of claim1 ~~to 21~~, wherein the linkage between the cationic molecules is degradable under cellular conditions.

23. The transfection particle of claim 1 which comprises a single nucleic acid molecule.

24. The transfection particle of claim 1 or 23, wherein the nucleic acid molecule is a DNA molecule.

25. The transfection particle of claim 24, wherein the DNA molecule is a plasmid.

26. The transfection particle of claim 1, wherein the nucleic acid molecule is an RNA molecule.

27. The transfection particle ~~of any one of~~ claims 1 ~~to 26;~~ characterized in that it carries one or more cellular targeting functions and/or one or more functions capable of facilitating endocytosis.

28. The transfection particle of claim 27, wherein said functions are linked to the cationic molecules.

29. The transfection particle of claim 27, wherein said functions are linked to nucleic acid binding molecules that are present in addition to the cationic molecules.

30. The transfection particle of claim 27, wherein the targeting function is a cellular protein ligand.

31. The transfection particle of claim 27, wherein the targeting function is a sugar residue.

32. The transfection particle of claim 31, wherein the sugar is galactose.

33. The transfection particle of claim 31, wherein the sugar is mannose.

34. The transfection particle of claim 1, characterized in that it carries one or more endosomolytic functions.

35. The transfection particle of claim 34, wherein said endosomolytic functions are linked to the cationic molecules.

36. The transfection particle of claim 34, wherein said functions are linked to nucleic acid binding molecules that are present in addition to the cationic molecules.

37. The transfection particle of claim 34, wherein the endosomolytic function is a fusogenic peptide.

38. The transfection particle of claim 34, wherein the endosomolytic function is a virus.

39. The transfection particle of claim 38, wherein the virus is an adenovirus.

40. A method for preparing transfection particles of ~~any of~~ claim~~s~~ 1 ~~to 39,~~ wherein cationic precursor molecules are added to nucleic acid molecules in a suitable buffer, allowed to form complexes with the nucleic acid and allowed to covalently link to identical or different cationic precursor molecules on the nucleic acid template.

41. The method of claim 40, wherein the cationic precursor molecules are lipophilic and are allowed to covalently link under mild oxidative conditions.

42. A pharmaceutical composition comprising a pharmaceutically effective amount of the transfection particle of claim 1, wherein the nucleic acid molecule is therapeutically active.

43. The pharmaceutical composition of claim 42, wherein the nucleic acid molecule is a plasmid encoding a therapeutically active protein.

44. A method for introducing therapeutically active nucleic acid into a mammal, wherein a transfection particle of claim 1 is administered to said mammal intradermally.

45. A kit of parts comprising one or more nucleic acid molecules, one or more cationic precursor molecules, suitable buffers, and other reagents or mechanical devices that are useful for preparation, purification and *in vitro* or *in vivo* application of a transfection particle of ~~any one of the~~ claims 1 ~~to 39.~~

46. The kit of parts of claim 45 comprising in addition or more functions for cellular targeting.

47. The kit of parts of claim 45 comprising in addition once or more endosomolytic functions.

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